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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,746	01/16/2001	Gunter Schmidt	PM 0276611	7741

909 7590 10/06/2004

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,746	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10-31 and 35-39* is/are pending in the application.

4a) Of the above claim(s) *3,13-19,23-30 and 35-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-6, 8, 10-12, 20-22 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed July 6, 2004 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 1-39 were pending. Applicants canceled claims 7, 9, 32-34 and amended claims 1, 5, 6, 8, 10, 12, 13 and 20. Therefore, claims 1-6, 8, 10-31 and 35-39 are currently pending.

4. Claims 3, 13-19, 23-30 and 35-39 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.

5. Therefore, claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are examined on the merits in this action.

Withdrawn Objections/Rejections

6. All outstanding objections to the specification and/or claims are withdrawn in view of Applicants' amendments. The rejection under 35 U.S.C. § 101 is withdrawn in view of Applicants' cancellation of claims. The rejections under 35 U.S.C. § 112, first paragraph are

withdrawn in part (i.e., with respect to methods that extend beyond mass spectroscopy, see below). The rejection under 35 U.S.C. § 112, second paragraph are withdrawn in view of Applicants' amendments and/or arguments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph - maintained

7. Claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method that employs "compounds disclosed in claim 11" wherein "R^1 is a trifluoroacetyl group or methyl sulfate", does not reasonably provide enablement for a method that employs "any" compound containing the formula shown in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is an enablement rejection.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) Breadth of the claims and nature of the invention: The claims are drawn to a broad genus. The scope of this claim includes an infinite number of methods for providing and using an infinite number of compounds (i.e., structural variants of the formula represented in claim 1). Consequently, the nature of the invention cannot be fully determined because the invention has not been defined with particularity.

(3 and 5) The state of the prior art and the level of predictability in the art: The instant specification only provides guidance to permit one of skill in the art to use compounds shown in claim 11 wherein R^1 = trifluoroacetyl group or methyl sulfate would be enabled because only these compounds possess a labile proton beta to the nitrogen that can support a negative charge as indicated in figure 9 to permit the facile release of the marker group for detection in a mass spectrometer. The Examiner further notes that Applicants do not provide any guidance for any other detection methods than mass spectroscopy.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants' examples only involve compounds that contain the formula shown in claim 11 wherein R^1 is a trifluoracetyl group or methyl sulfate i.e., an electron withdrawing group that will stabilize the negative charge that forms on the atom γ to the SO_2 group (e.g., see figures 3, 9 and 15). In addition, Applicants provide examples for

the use of protein analytes via a cysteine (e.g., see specification page 13, last paragraph) or serine, threonine and/or tyrosine (e.g., see specification page 22, last paragraph), but do not provide any examples for other class of analytes including pharmaceuticals, inorganic complexes, etc. Finally, Applicants specification also only provides examples of mass labels that contain a $-S(=O)_2-Ar$ group (e.g., see figure 1-18) and, as a result, this appears to be an "essential" feature of the invention. A claim is non-enabled under 35 U.S.C. 112, first paragraph, if the claim lacks critical or essential disclosed elements which are necessary to practice of the invention. See In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of

success and the practice of the full scope of the invention would require undue experimentation.

Response

8. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "With respect to the breadth of claim 1, it is submitted that the compounds falling within the scope of amended claim 1 are now defined with sufficient particularity. The R group of claim 1 has been limited to S, SO, NR_1, or O between the C atom that is in the β-position to the SO_n group and the reporter group or analyte. This limitation defined the cleavage point of the compound, which releases the reporter group for characterization by mass spectrometry" (e.g., see 7/6/04 Response, page 11, paragraph 2).

[2] Applicants argue, "a person skilled in the art would not require undue experimentation in order to be able to use the methods of the present invention. Specific examples of compounds falling within the scope of amended claim 1 may be found in the figures for the present application. As discussed above, the reporter grouped does not need to be particularly limited provided that it is readily detectable and can be related to analyte in order to identify the analyte" (e.g., see 7/6/04 Response, page 11, paragraph 3).

This is not found persuasive for the following reasons:

[1] The Examiner contends that Applicants amendments do not fully address the issue because as stated in the rejection above, "The instant specification only provides guidance to permit one of skill in the art to use compounds shown in claim 11 wherein R^1 = trifluoroacetyl group or methyl sulfate would be enabled because only these compounds possess a labile proton beta to the nitrogen that can support a negative charge as indicated in figure 9 to permit the facile release of the marker group for detection in a mass spectrometer" (see rejection above, elements 3 and 5). In addition, the Examiner also noted, "Applicants' examples only involve compounds that contain the formula shown in claim 11 wherein R^1 is a trifluoracetyl group or methyl sulfate (e.g., see figures 3 and 15)" and thus it is unclear how other groups, say an electron donating group, would work at the R1 position because the negative charge that is formed upon cleavage would not be stabilized.

[2] The Examiner contends that undue experimentation would be required as exemplified by the Wands factors above (e.g., see above rejection). In addition, the Examiner notes that a "representative" number of examples are not provided. For example, Applicants' do not provide an example of an R1 group that is electron donating and the Examiner does not see how such a group could be used because it would destabilize the negative charge that is built up on the nitrogen during fractionation (e.g., see claim 11; see also figure 9). In addition, it is not clear to the examiner how, for example, an "NMR" reporter could be used in a "mass spectrometer" to identify said ligand.

Accordingly, the Enablement rejection cited above is hereby maintained.

9. Claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicants' claims are directed to a method for characterizing an "analyte" using a "cleavable linker" and a "reporter" molecule that is covalently attached to said analyte via the cleavable linker (e.g., see newly amended claim 1), which represents enormous scope because Applicants do not place any limit on the structure of the analyte (i.e., could be organic, inorganic, small, large, biological, non-biological, etc.) or the reporter group (conceivable any molecule would fall within this scope as long as it could be monitored by a physical technique e.g., NMR, mass spectrometry, fluorescence, etc.). In addition, Applicants' claimed linker also provides for an enormous number of variants because each of the variables described in the linker (e.g., see claim 1) can be independently varied along with the analyte and the reporter molecule. Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope.

In contrast, Applicants' specification provides only one example of a reporter molecule (e.g., see figures 1-18 wherein an Ar-S(=O)$_2$- group is shared between all disclosed examples) and only one class of analytes i.e., Applicants' claims seem to be drawn only to proteins (e.g., specification, page 13, last paragraph, see also page 22, last

paragraph; see also pages 41-43 wherein Applicants provide guidance for coupling to a class of "protein" analytes via cysteine, threonine, etc.). In addition, Applicants provide only linkers that contain the formula shown in claim 11 wherein R^1 is a trifluoracetyl group or methyl sulfate i.e., to stabilize the negative charge that forms on the atom γ to the SO_2 group during cleavage (e.g., see figures 3, 9 and 15)

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, Applicants have not provided only a limited number of examples (see above) that are not commensurate with the broad scope of the claimed invention. Consequently, one of skill in the art would reasonably conclude that Applicants were not in possession of the full scope of the claimed invention.

Furthermore, the general knowledge and level of skill in the art would not permit Applicants' to extend their limited teaching to the full scope of the claimed invention because the genus that is currently claimed is enormous and highly variable (e.g., the currently claimed invention encompasses molecules in all classes and subclasses). Thus, listing examples like FT134 (e.g., see specification, figure 11) in the specification is insufficient to teach the entire genus. In addition, the instant specification only provides guidance to permit one of skill in the art to make and/or use compounds shown in claim 11 wherein R^1 = trifluoroacetyl group or methyl sulfate since these compounds possess a labile proton beta to the nitrogen that can support a negative charge as indicated in figure 9 to permit the facile release of the marker group for detection in a mass spectrometer.

Response

10. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "the person skilled in the art would be able to clearly identify compounds that fall within the scope of the invention .... the skilled person does not require any structural features of the analyte or the reporter group in order to determine which compounds fall within the scope of amended claim 1" (e.g., see 7/6/04 Response, paragraph bridging pages 11-12).

[2] Applicants argue, "the specification discloses a number of examples of compounds falling within the scope of amended claim 1" (e.g., see 7/6/04 Response, page 12, paragraph 1).

[3] Applicants argue, "the examiner's concerns ... seem not to lie in whether the claims have written description support, but rather in the alleged lack of guidance from the specification ... applicants respectfully request that the examiner address these issues in an enablement rejection, not a written description rejection" (e.g., see 7/6/04 Response, page 12, paragraph 2).

This is not found persuasive for the following reasons:

[1] The Examiner contends that the "indefiniteness" is not at issue in this rejection i.e., the claims are not being rejected under 35 U.S.C. 112, second paragraph and, as a result, Applicants' arguments are moot.

[2] The Examiner contends that the examples provided by Applicants are not "representative" of Applicants' broad scope for the reasons outlined in the above rejection.

[3] The Examiner contends that written description is legally distinct from enablement and must be addressed in its own section: "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30,2001) citing *University of California v. Eli Lilly &Co.* In addition, the Examiner notes that the amount of "guidance" in the specification speaks to both issues i.e., whether Applicants have provided a "representative" number of species as required by *Lilly*.

Accordingly, the written description rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 102 - maintained

11. Claims 1, 2, 4-6, 8, 10-12, 20 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Nothnagel (Nothnagel, E. A. "Synthesis and characterization of fluorescent Lucifer yellow-lipid conjugates" Biochimica et Biophysica Acta **1989**, 980(2), 209-219).

For ***claim 1***, Nothnagel (see entire document) disclose methods for synthesizing and using fluorescent Lucifer yellow-lipid conjugates (see Nothnagel, abstract), which anticipates claim 1. For example, Nothnagel disclose providing a compound in which the analyte is attached by a cleavable linker to a reporter group relatable to the analyte having the formula shown in claim 1 (e.g., see Nothnagel, figure 1, schematic B showing a compound with formula LY-SO_2-CH_2-CH_2-$DC_{12:0}$PE). In this scenario, the Lucifer Yellow Dye ("LY") represents the "reporter" and the $DC_{12:0}$PE represents the "analyte." further disclose cleaving the reporter group from the analyte (e.g., see Nothnagel, figure 2 wherein the $DC_{12:0}$PE "analyte" is cleaved from the LY "reporter" via FAB-MS i.e., the peak at 578 corresponds to the "cleaved" $DC_{12:0}$PE analyte peak). Finally, Nothnagel disclose identifying the reporter group, thereby characterizing the analyte (e.g., see Nothnagel, figure 2 wherein the parent ion and fragment ions that contain the FY reporter are "identified" and used to "characterize" the lipid analyte via comparison of molecular weights). Please note that there are many other variations for the analyte and/or reporter that also read on Applicants' claims. For example, the "analyte" could be a "12:0 fatty acid side chain" instead of the $DC_{12:0}$PE mentioned above or the phoshphatidic acid

portion ("PA") of the molecule (e.g., see Nothnagel, figure 2 wherein the peaks at 946 and 346 represent "lyso" derivatives of $DC_{12:0}PE$ wherein fatty acid side chain "analytes" are cleaved from the reporter).

For ***claim 2***, Nothnagel disclose a covalent linkage between the analyte and/or reporter group and the cleavable linker (e.g., see figure 2 showing the cleavage of a covalent bond when the DC12:0PE signal is generated at mass 578).

For ***claim 4-6***, Nothnagel disclose a substituted phenyl wherein R^2, R^4, R^5 and R^6 are hydrogen and R^3 is LY (e.g., see Nothnagel, figure 1, scheme B wherein a phenyl ring connects the LY to the SO_2-CH_2-CH_2-$DC_{12:0}PE$ i.e., LY-phenyl-SO_2-CH_2-CH_2-$DC_{12:0}PE$).

For ***claim 8***, Nothnagel disclose -NR^1- wherein R^1 is a hydrogen (e.g., see Nothnagel, figure 1, scheme B showing -SO_2-CH_2-CH_2-N(H)-CH_2-CH_2-).

For ***claims 11-12***, Nothnagel disclose LY-phenyl-SO_2-CH_2-CH_2-N(H)-CH_2-CH_2-$DC_{12:0}PA$ wherein "PA" represents the phosphatidic acid portion of the molecule (e.g., see Nothnagel, figure 1, scheme B). In this scenario, X' is PA, the "handle" connecting PA to N-R^1 is -CH_2-CH_2-, R^1 is hydrogen, the "handle" connecting SO_2 to X is a covalent bond and X is LY. Please note that claim 12 has been interpreted as depending on claim 11.

For ***claims 20 and 31***, Nothnagel disclose detecting the reporter using FAB-MS and its cleavage products (e.g., see Nothnagel, figure 2).

Response

12. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "Nothnagel does not disclose a method for characterizing an analyte according to claim 1 of the present invention" (e.g., see 7/6/04 Response, pages 13-14).

[2] Applicants argue, "The compound of figure 1B [referring to Nothnagel, page 211] represents the whole probe which is used to label cell membranes. The applicants do not agree with the examiner's opinion that the Lucifer Yellow Dye (LY) part represents the reporter group and the DC12:0PE part represents the analyte" (e.g., see 7/6/04 Response, page 14, second paragraph).

[3] Applicants argue, "Figure 2 may disclose the uncontrolled cleavage of $DC_{12:0}PE$ from LY by FAB mass spectrometry used to analyze the whole probe. However, this is not the same as the specific step of cleaving the reporter group from the analyte according to the present invention wherein the compound, at a particular point, is cleanly cleaved into two parts. In contrast, the probe in Nothnagel is cleaved into many different parts and does not split the compound in the correct place" (e.g., see 7/6/04 Response, page 14, paragraph 3).

[4] Applicants argue, "Nothnagel does not disclose the characterization of an analyte by identification of a reporter group. The FAB mass spectrometry used in Nothnagel was used to

characterize and identify the whole probe not to identify the FY part of the probe to characterize the $DC_{12:0}PE$ part of the probe" (e.g., see 7/6/04 Response, page 14, paragraph 4).

[5] Applicants argue, "The FAB mass spectrometry used in Nothnagel was used to characterize and identify the whole probe not to identify the FY part of the probe to characterize the $DN_{12:0}PE$ part of the probe" (e.g., see 7/6/04 Response, page 14, paragraph 4).

[6] Applicants argue, "Figure 2 in Nothnagel does not show a mass ion peak for LY, which would suggest that LY is not used as a reporter group" (e.g., see 7/6/04 Response, page 14, paragraph 4).

[7] Applicants argue, "Nothnagel does not disclose that the mass-to-charge ratio of the reporter group is determined to identify the analyte as recited in amended claim 1" (e.g., see 7/6/04 Response, page 14, paragraph 4)

This is not found persuasive for the following reasons:

[1] The Examiner contends that Nothnagel does disclose the characterization of an analyte as outlined in the amended rejection above (see also section **[2]** below). In addition, the Examiner contends that Applicants' arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. Here, Applicants describe a feature of the Nothnagel reference, but fail to provide how this feature distinguished from the claimed invention i.e., why the use of a fluorescent lipid probe composed of Lucifer yellow dyes linked to either cholesterol or phospholipids for use in labeling does not fall within the scope of characterizing an analyte.

[2] The Examiner respectfully disagrees. For example, figure 6B and 6C show the "internalization" of an "analyte" into the cell (e.g., compare figures 6B to 6C on page 216 wherein figure 6B shows a greater internalization for the $DC_{18:2}PE$ than is shown in figure 6C for the $DC_{16:0}PE$; see also figure 6E wherein the comparison is made to cholesterol; Please note that the same reporter, LY, is used in each case proving that the lipid and/or cholesterol moiety is the focus of the investigation). Here, Nothnagel is "testing" or "analyzing" whether the $DC_{18:2}PE$ will be internalized to a greater or lesser extent than the $DC_{16:0}PE$. Thus, the LY reporter in these experiments is used solely for the purpose of identifying the analyte under investigation i.e., the lipid (e.g., see also page 218, column 1, last paragraph). Other examples include monitoring the diffusion rates of lipids in cell membranes (e.g., see Table II wherein the lipid analyte is varied and the LY reporter is held constant).

[3] The Examiner contends that Applicants' arguments are not commensurate in scope with the claims. For example, Applicants use of "comprising terminology" does not preclude the probe from being cleaved into many different parts. In addition, in response to applicants' arguments that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (e.g., "controlled cleavage", "cleanly cleaved into two parts", "splitting the compound in the correct place") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

[4] The Examiner respectfully disagrees. The analyte was "characterized" by both "mass spectrometry" and "fluorescence" measurements. If mass spectrometry was not used to

characterize the structure of the LY reporter – Lipid and/or cholesterol analyte structure then the subsequent fluorescent experiments (e.g., see figure 6) would not have any meaning because the experimenter would not be able to tell whether the fluorescent signal was due to the LY reporter alone or to a LY reporter – lipid conjugate (i.e., mass spectrometry characterizes the analyte as a conjugate). Thus, both "mass spectrometry" and "fluorescence spectroscopy" must be used "together" in characterizing said analyte because fluorescence spectroscopy alone cannot establish the structure of the analyte when it is covalently attached to said reporter. The Examiner further notes that Applicants' use of "comprising" terminology does not preclude the use of more than one technique to "characterize" the analyte.

In addition, the Examiner notes that "identifying" lower mass peaks that contain the "reporter group" i.e., fragmentation analysis (e.g., see figure 2B wherein the Lyso-LY-$DC_{12:0}PE$ fragment was "identified" at 946) is a common method for "characterizing" other portions of the molecule including the "analyte" in this case because said lower mass peaks can be used to prove the structure of the analyte directly (e.g., analysis of 946 peak shows that an "intact" analyte was covalently coupled to the reporter) or indirectly by subtraction from the parent ion (i.e., parent ion identification – reporter ion identification → analyte ion characterization whether the analyte ion is actually observed or not) (e.g., see figure 1B wherein the "reporter" peak at 450 can be subtracted from the parent ion at 856 to "characterize" the analyte ion after the Li and H counter ions are taken into consideration).

[5] The Examiner contends that Applicants' arguments are not commensurate in scope with the claims. Applicants' use of "comprising terminology" does not preclude the identification of the "whole" probe as Applicants purport.

[6] The Examiner respectfully disagrees. Figure 2 does show a mass ion peak for LY (e.g., the parent ion contains LY at 1128 and the lyso-LY-DC12:0PE at 946 contain LY). In addition, a peak at 450 corresponds to LY in figure 2A that shows that LY can act as a "reporter" by itself or in conjunction with smaller fragments of the analyte in fragmentation analysis. In addition, LY is clearly functioning as a reporter in the fluorescence measurements in figure 6 and nothing in Applicants' claims precludes the reporter group from functioning as a fluorescent label instead of a mass label or as both.

[7] In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "mass-to charge ration of the reporter group is determined to identify the analyte") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In addition, the Examiner notes that the mass-to-charge reaction was used to identify the reporter when the peak at 946 was characterized (i.e., see figure 2B wherein the peak at 946 corresponds to both the label and the lyso-analyte).

Accordingly, the 35 U.S.C. §102 rejection cited above is hereby maintained.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
October 2, 2004

BENNETT CELSA
PRIMARY EXAMINER